Universal Pluripotent Liver Failure Therapy (UPLiFT)

Grant Award Details

Universal Pluripotent Liver Failure Therapy (UPLiFT)

Grant Type: Quest - Discovery Stage Research Projects

Grant Number: DISC2-10979

Investigator:

Name:	Tracy Grikscheit
Institution:	Children's Hospital of Los Angeles
Type:	PI

Disease Focus: Liver Disease, Metabolic Disorders

Human Stem Cell Use: iPS Cell

Award Value: $1,297,512

Status: Pre-Active

Grant Application Details

Application Title: Universal Pluripotent Liver Failure Therapy (UPLiFT)

Public Abstract:

Research Objective

Universal Pluripotent Liver Failure Therapy (UPLiFT) is composed of 2 lines- UPLiFT0 (from LiPSC-GR1.1) and UPLiFT1 which will be derived from gene edited universal human pluripotent stem cells.

Impact

In some liver-based metabolic diseases, replacement of 5-10% of the liver mass may salvage the patient. Transplantation of hepatic progenitors from universal donor cells might avoid immunosuppression.

Major Proposed Activities

- Developing and testing a cGMP-compliant manufacturing protocol for differentiating LiPSC-GR1.1 and the gene edited universal version of these cells into hepatic progenitors.
- Production of sufficient cells of UPLiFT0 (LiPSC-GR1.1) and UPLiFT1 (Universal donor) sufficient to perform Milestones 3-5 including mouse studies
- UPLiFT Function and Fate: In our established in vivo model of hepatic stem/progenitor cell transplantation, assess the maturation, proliferation, and function of transplanted hepatic progenitor cells
- Select dose, determine regiment and route of administration. In tested model of hepatic failure establish effective dose and regimen
- Pilot preclinical safety/toxicology/long term outcomes at the optimal dose and route, assess off-target effects.
- Preparation of Pre-Pre IND Package and Scheduling/Conduct of Pre-Pre IND meeting

Statement of Benefit to California:

California has the 12th highest death rate of liver disease in the US. The worldwide burden of liver disease is around 30 million patients, affecting one in ten in the US. Liver-based metabolic diseases are a rational starting point to apply cellular therapy to liver disorders. In some congenital metabolic disorders, replacement of 5-10% of the native liver mass may salvage the patient from the buildup of toxic metabolites. Our proposed cell therapy might expand treatment options.

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